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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,945	05/02/2001	Neil P. Desai	ABI1460-3 (071243-1317)	6174

30542 7590 05/19/2003

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EXAMINER
GOLLAMUDI, SHARMILA S

ART UNIT	PAPER NUMBER
1616	15

DATE MAILED: 05/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/847,945	DESAI ET AL.	
	Examiner	Art Unit	
	Sharmila S. Gollamudi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Peri d for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *2/24/03* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *13* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Receipt of Information Disclosure Statement received on December 12, 2002 and Amendment A received on February 24, 2003 is acknowledged. Claims 1-30 are included in the prosecution of this application.

Response to Amendment

Applicant's arguments have been considered but are moot in view of the new ground(s) of rejection in view of amendment.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 18, 20-25, and 26-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Grinstaff et al (5,498,421).

Grinstaff et al teach encasing a water-insoluble biologically active agent in a polymeric shell (microparticles) for in vivo delivery. See abstract and column 1, lines 60-64. The delivery of the actives in the form of microparticles allows for targeting organs for treatment, increased stability of the insoluble active agent compared to simple emulsions, emulsifier-free system and solubilizer-free system wherein allergic reactions are reduced, and the use of small doses. See column 7, lines 15-26. Grinstaff teaches protein as suitable biocompatible materials for the formation of the polymeric shell. See column 8, lines 36-68. The active agents that may be incorporated into the polymeric

shell are taxols and camptothecin. See column 14, lines 1-6. Example 6 demonstrates the reduced toxicity of the drugs in the polymeric shells.

*Note the rejected claims recite intended use. For instance, the recitation a composition "for reducing hyperplasia associated with vascular interventional procedure" does not hold patentable weight unless the intended use provides a structural limitation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-15 and 17-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kunz et al (5,733,925) in view of Grinstaff et al (5,498,421).

Kunz et al teach methods for inhibiting stenosis following vascular trauma or disease, cancer, diseases resulting from hyperactivity or hyperplasia of somatic cells. Kunz teaches direct or targeted delivery of therapeutic agents to vascular smooth

muscle cells. See column 1, lines 15-35. Inhibiting stenosis following angioplasty is contemplated. See column 3, lines 54-62. The dosage forms are preferably in biodegradable microparticulates or nanoparticulates wherein the particles are formed of a polymer-containing matrix that biodegrades. Therapeutic agents such as taxol or analogs are preferred therapeutic agents that are designed to target the cell activity without killing the cell. Taxol is taken into the cell and stabilizes the cell from further dividing. See column 4, lines 40-45 and column 13, lines 24-27. Kunz et al teach conjugating the drug with a binding protein to target the cells. See column 14, lines 25-33. The reference teaches that s skilled practitioner may determine the optimal and effective does and provides guidance which allows one to judge if a therapeutically effective dosage has been reached on column 30, lines 6-20. Examples of dosages include .01 to 10 mg/kg per day. See column 29, lines 10-15. Delivery of the active agents may be intravenous, intraaterial (stents), or local delivery. See column 30, lines 56-65.

Although Kunz et al teach the therapeutic agent conjugated to a protein for targeting cells, Kunz does not teach a protein coated active agent.

Grinstaff et al teach encasing a water-insoluble biologically active agent in a polymeric shell (microparticles) for in vivo delivery. See abstract and column 1, lines 60-64. The delivery of the actives in the form of microparticles allows for targeting organs for treatment, increased stability of the insoluble active agent compared to simple emulsions, emulsifier-free system and solubilizer-free system wherein allergic reactions are reduced, and the use of small doses. See column 7, lines 15-26. Grinstaff teaches

protein as suitable biocompatible materials for the formation of the polymeric shell. See column 8, lines 36-68. The active agents that may be incorporated into the polymeric shell are taxols and camptothecin. See column 14, lines 1-6. Example 6 demonstrates the reduced toxicity of the drugs in the polymeric shells.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Kunz et al and Grinstaff et al and coat the active agent with a protein coating. One would be motivated to do so since Kunz teaches that taxane drugs treat stenosis due to various conditions such as hyperplasia (defined as a proliferative disease) and Grinstaff teaches drugs that treat proliferative diseases such as paclitaxel are insoluble drugs and coating the drugs with a coating such as protein allows for a stable pharmaceutical composition, which reduce side effects such as allergies. Furthermore, Grinstaff teaches protein-coated drugs provide targeting of organs.

Claims 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kunz et al (5,733,925) in view of Grinstaff et al (5,498,421) in further view of Li et al (5,977,163).

As set forth above, Kunz et al teach methods for inhibiting stenosis following vascular trauma or disease, cancer, diseases resulting from hyperactivity or hyperplasia of somatic cells. Therapeutic agents such as taxol or analogs are preferred therapeutic agents that are designed to target the cell activity without killing the cell. Taxol is taken into the cell and stabilizes the cell from further dividing. See column 4, lines 40-45 and column 13, lines 24-27. Delivery of the active agents may be intravenous, intraaterial

(stents), or local delivery. Grinstaff et al teach protein coated active agents such as taxane drugs.

Although Kunz teaches intraaterial administration, neither reference specifies coating a stent with the drug.

Li et al teach paclitaxel compositions used in the treatment of cancer and restenosis (stenosis) of vessels subjected to stenting or angioplasty. See column 2, lines 24-35. Li teaches the coating stents with drug-polymer compositions to inhibit smooth muscle cell proliferation. See column 6, lines 1-43.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Kunz et al, Grinstaff et al, and Li et al and use a coated stent to treat hyperplasia. One would be motivated to do so since Li et al teaches the state of the art at the time the invention was made to use coated implants to treat stenosis due to proliferative diseases. Furthermore, one would expect similar results since Kunz teaches that taxane compounds treat stenosis due to various diseases such as cancer and hyperplasia.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is (703) 305-2147. The examiner can normally be reached on M-F (7:30-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jose Dees can be reached on (703) 308-4628. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

SSG
May 15, 2003

MICHAEL G. HARTLEY
PRIMARY EXAMINER